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CHEMISTRY

Synthesis and Testing of Abscisic Acid with Predominant Replacement of Protium Atoms by Tritium in the Cyclohexene Moiety

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Abstract—A procedure for tritiation of predominantly the cyclohexene moiety of abscisic acid was developed. Tritium was introduced by isotope exchange reaction with 100% tritiated water at 220°C in the presence of diisopropylethylamine. The yield of abscisic acid was 50%, and the specific activity was 30.5 Ci/mmol. The labeled product was tested. It was shown that tritiated abscisic acid synthesized by the proposed method did not differ from the unlabeled precursor and could be used for biological assays.

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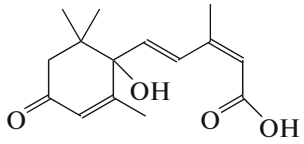
The biological activity of abscisic acid (ABA) has been studied for many years [1, 2]. It inhibits the growth of various parts of plants and seed and tuber sprouting and plays an important role in the plant adaptation to harsh environment. The use of tritium-labeled abscisic acid facilitates the studies along this line.

A method for tritium labeling of the acyclic part of the ABA molecule has been reported [3]. According to this procedure, tritium was introduced into the precursor by selective acetylene bond hydrogenation. In the developed method, tritium enters mainly the cyclohexene moiety of the ABA molecule. Unlike tritiation by chemical methods (chemical synthesis, hydrogenation, dehalogenation, etc.), isotope exchange methods allow the most precise optimization of the reaction conditions. This approach to isotope labeling is the subject of quite a number of scientific papers and reviews [4–6].

Most often, tritium is introduced via isotope exchange with tritium gas or tritiated water. The use of tritium gas for isotope labeling of unsaturated compounds is of low utility, since the isotope exchange is minimized and hydrogenation of the starting compound is the major reaction.

Operations with 100% tritiated water are usually carried out using heterogeneous catalysts that are stable to radiolysis and thus do not generate additional difficulties for the isolation of labeled products from reaction mixtures [7, 8]. As follows from published data, the conditions of choice for isotope exchange with tritiated water are as follows: tritiated water concentration of 2–3% and palladium oxide pre-reduced with tritium gas as the source of tritiated water. Dioxane is used as the solvent in most cases.

Since the cyclohexene part of the abscisic acid molecule bears a keto group, the tritium labeling of ABA via isotope exchange with tritiated water should reasonably be base-catalyzed:



In this case, isotope exchange will occur most efficiently at the α-positions of the keto group and the greater part of tritium will enter the cyclohexene moiety of the ABA molecule. In addition, some tritium will be introduced into the methyl groups of the ring, which would also increase the degree of labeling of the cyclohexene moiety. Therefore, the attention was focused on the base-catalyzed isotope exchange with tritiated water [9]. The bases used for this purpose include sodium methoxide, KOH, diazabicycloundecene, Et_3N, butyllithium, etc. [10–13]. Under these conditions, dilution of tritiated water with protium of the medium is minimized.

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